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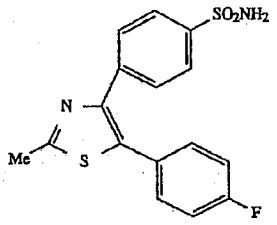
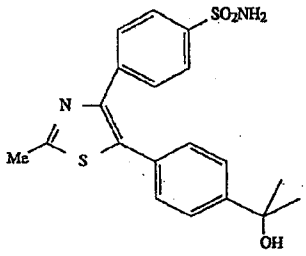
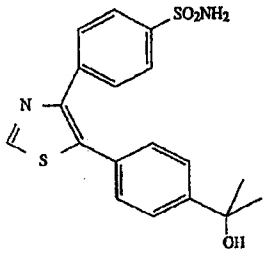
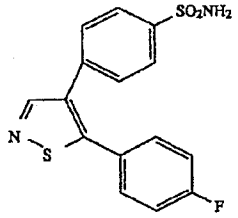
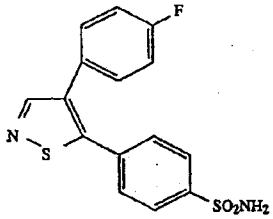
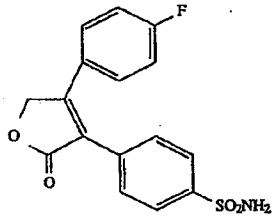
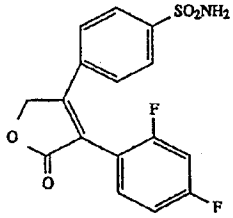
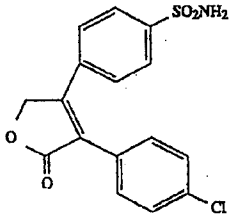
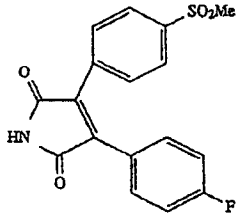
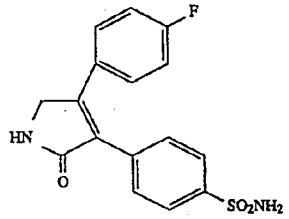
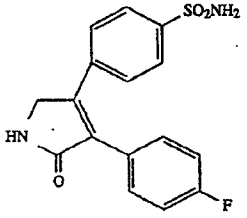
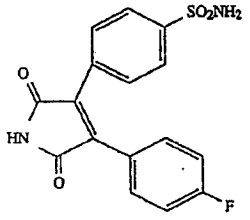
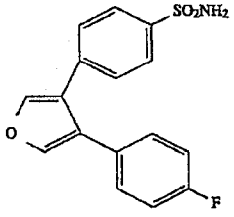
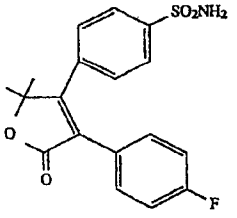
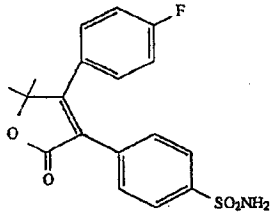
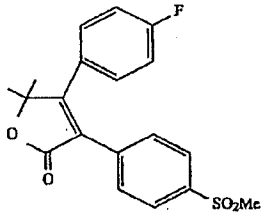
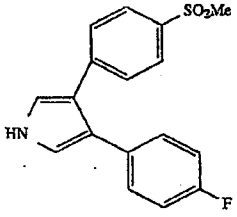
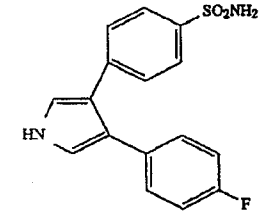

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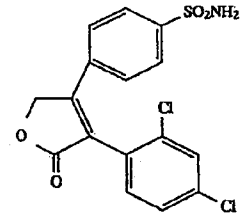
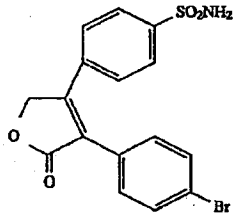
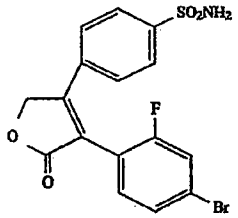
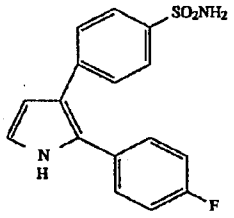
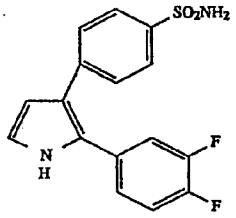
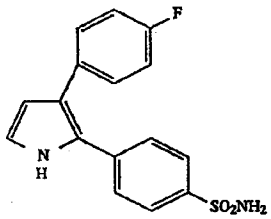
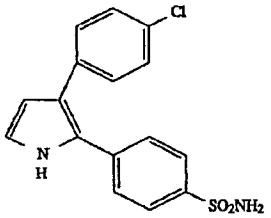
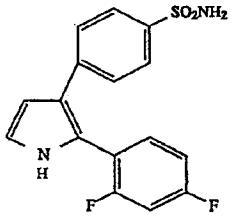
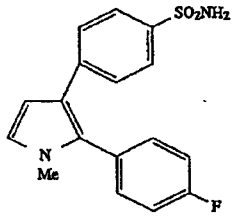
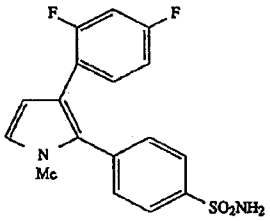
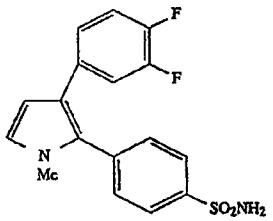
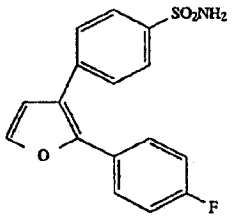
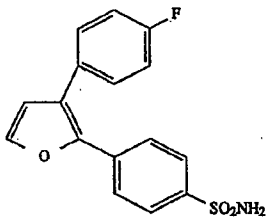
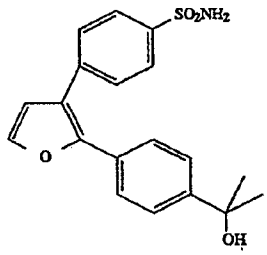
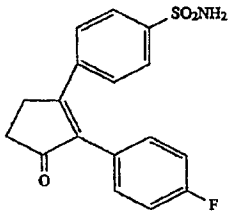
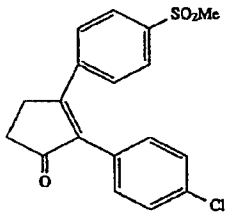
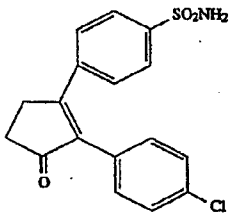

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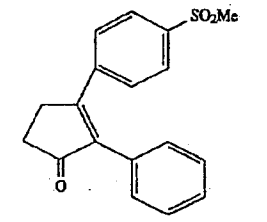
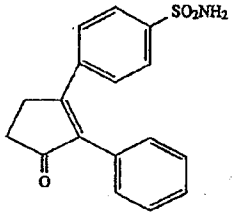
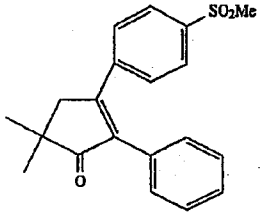
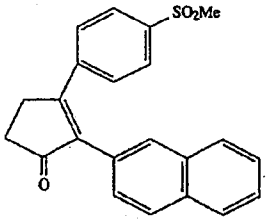
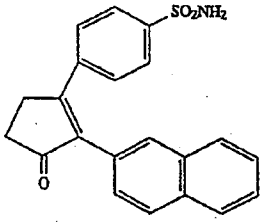
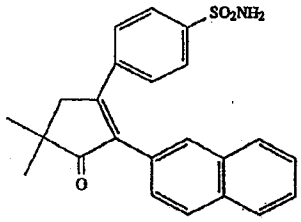
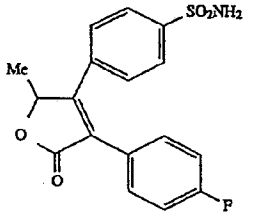
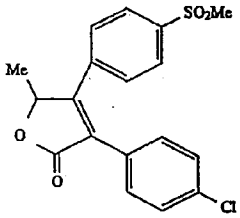
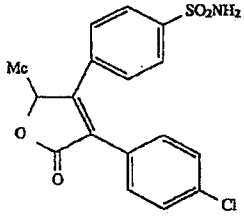
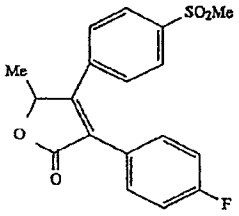
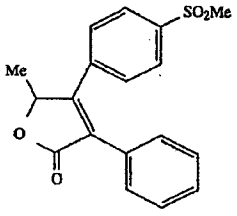
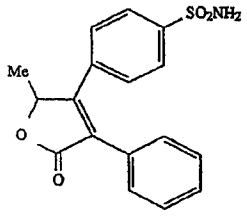
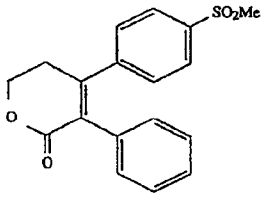
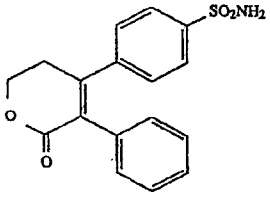
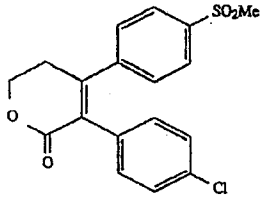
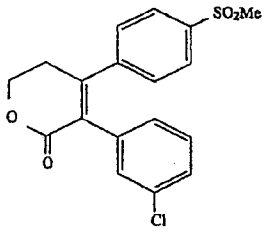
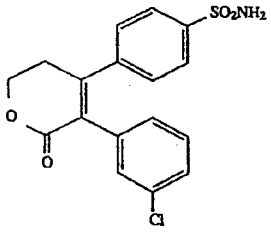
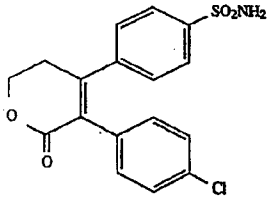

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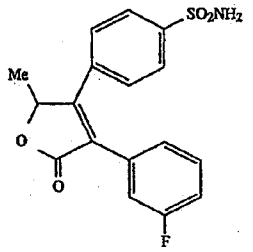
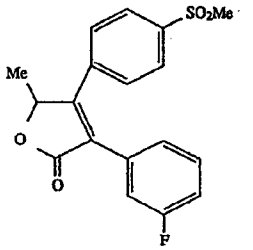
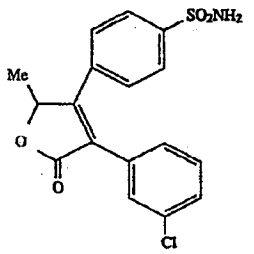
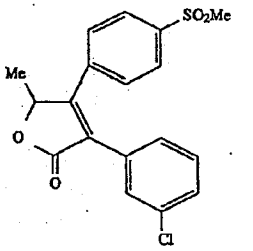
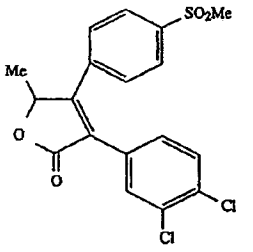
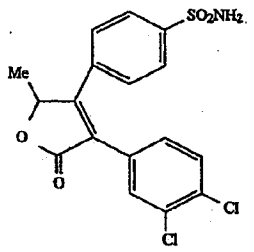


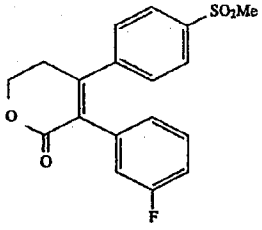


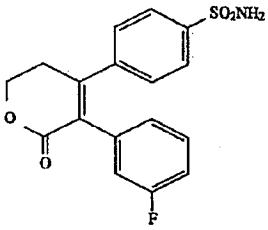


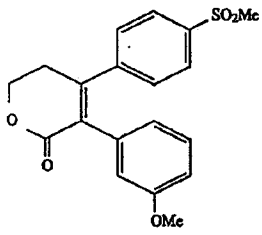


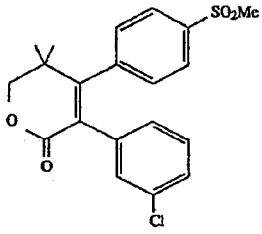


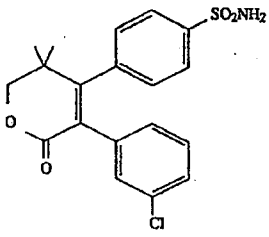


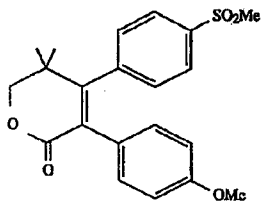


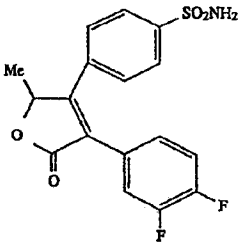


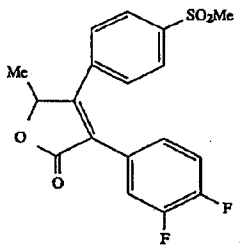












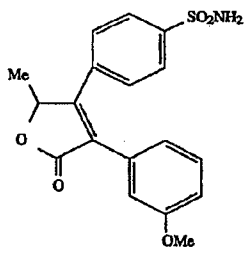
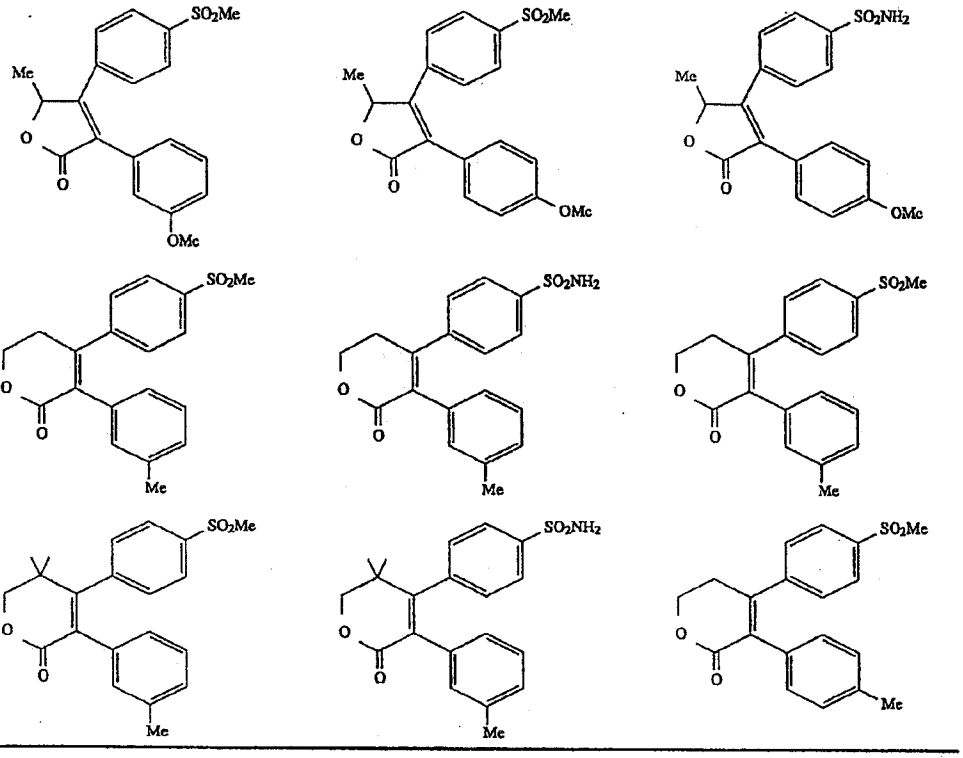


TABLE II-continued



Assays for Determining Biological Activity

The compound of Formula I can be tested using the following assays to determine their cyclooxygenase-2 inhibiting activity.

Inhibition of Cyclooxygenase Activity

Compounds were tested as inhibitors of cyclooxygenase activity in whole cell and microsomal cyclooxygenase assays. Both of these assays measured prostaglandin E_2 (PGE_2) synthesis in response to arachidonic acid, using a radioimmunoassay. Cells used for whole cell assays, and from which microsomes were prepared for microsomal assays, were human osteosarcoma 143 cells (which specifically express cyclooxygenase-2) and human U-937 cells (which specifically express cyclooxygenase-1). In these assays, 100% activity is defined as the difference between prostaglandin E_2 synthesis in the absence and presence of arachidonate addition. IC_{50} values represent the concentration of putative inhibitor required to return PGE_2 synthesis to 50% of that obtained as compared to the uninhibited control. Representative results are shown in Table III.

Representative Rat Paw Edema Assay — Protocol

Male Sprague-Dawley rats (150–200g) were fasted overnight and were given to either vehicle (5% tween 80 or 1% methocel) or a test compound at 9–10 am. One hr later, a line was drawn using a permanent marker at the level above the ankle in one hind paw to define the area of the paw to be monitored. The paw volume (V_{0h}) was measured using a plethysmometer (Ugo-Basile, Italy) based on the principle of water displacement. The animals were then injected subplantarly with 50 ul of a 1% carrageenan solution in saline (FMC Corp, Maine) into the paw using an insulin syringe with a 25-gauge needle (i.e. 500 ug carrageenan per paw). Three hr later, the paw volume (V_{3h}) was measured and the increases in paw volume (V_{3h}–V_{0h}) were calculated. The animals were euthanized by CO_2 aphyxiation and the absence or presence of stomach lesions scored. Stomach scores were expressed as the sum of total lesions in mm. Paw edema data were compared with the vehicle-control group and percent inhibition calculated taking the values in the control group as 100%. Since a maximum of 60–70% inhibition (paw edema) was obtained with standard NSAIDs, ED_{30} values were used for comparison. All treatment groups were coded to eliminate observer bias. With this protocol, the ED_{30} for Indomethacin is 1.0 mg/kg. Representative results are shown in Table IV.

TABLE III*

Example	Whole Cells			Microsomes		
	Conc. (nM)	COX-2 % inhib.	COX-1 % inhib.	Conc. (nM)	COX-2 % inhib.	COX-1 % inhib.
1	100	96	12	100	53	8
2	10	69	0	10	49	25
3	10	42		10	33	19
3	100	100		100	76	12
4				10	47	2
5	10	0	0	10	43	31

TABLE III*-continued

Ex-	Whole Cells			Microsomes		
ample	Conc. (nM)	COX-2 % inhib.	COX-1 % inhib.	Conc. (nM)	COX-2 % inhib.	COX-1 % inhib.
6	100	78		100	19	16
7	100	74	0	1000	58	16
8	10	41				
8	100	89				
9	100	83		100	37	9
10	100	95		100	71	12
11	100	39		100	46	7
12	100	54				
13	10	41		10	52	7
13	100	84		10	58	10
14	10	73		10	45	29
14	100	89		100	63	0
14	1000	101		1000	69	0
15	20	39				
15	80	76				
15	160	95				
16	20	41				
16	40	50				
16	160	85				
17	40	41				
17	160	77				
18	40	24				
18	160	58				
19	40	21				
19	160	59				
20	10	70				
20	40	91				
21	10	50				
21	40	94				
22	20	39				
22	160	98				
23	20	50				
23	160	88				
24	40	43				
24	160	78				
25	160	40				
26	80	27				
26	160	39				
27	20	38				
27	160	97				
28	20	48				
28	160	69				
29	20	78				
29	160	85				
30	160	30				
31	20	49				
31	160	87				
32	5	43				
32	10	73				
32	40	92				
32	80	99				
33	160	6				
34	10	30				
34	40	80				
34	160	102				
35	20	32				
35	40	57				
35	160	83				
36	10	11				
36	40	50				
36	160	89				
37	10	53				
37	40	82				
37	160	93				
38	10	25				
38	40	63				
38	160	88				
39	10	17				
39	160	84				
40	10	43				
40	40	72				
40	160	96				
41						

TABLE III*-continued

Ex-	Whole Cells			Microsomes		
ample	Conc. (nM)	COX-2 % inhib.	COX-1 % inhib.	Conc. (nM)	COX-2 % inhib.	COX-1 % inhib.
41						
42	20	10				
42	160	44				
43	10	78				
43	40	101				
44	20	14				
44	40	55				
44	160	106				
45	10	16				
45	40	61				
45	160	101				
46	10	76				
46	40	94				
46	160	97				
47	10	61				
47	40	74				
47	160	101				
48	10	7				
48	160	47				
49	10	53				
49	40	91				
49	80	99				
50	80	42				
51	5	49				
51	20	95				
51	40	102				
52	10	50				
52	40	82				
52	160	102				
53	10	54				
53	40	96				
53	160	102				
54	10	81				
54	80	91				
54	160	99				
55	10	48				
55	80	59				
55	160	65				

*In the whole cell assay Ibuprofen has an IC50 for COX-1 of 1000 nM, and an IC50 for COX-2 of 3000 nM. Similarly, Indomethacin has an IC50 for COX-1 of 100 nM, and an IC50 for COX-2 of 10 nM.

TABLE IV

ED30(mg/kg)	STRUCTURE
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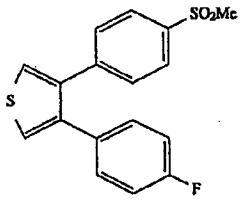
>10.00	

TABLE IV-continued

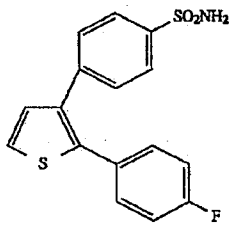
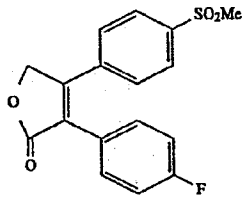
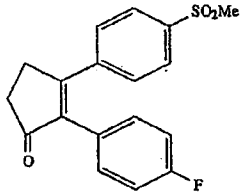
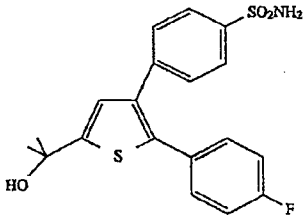
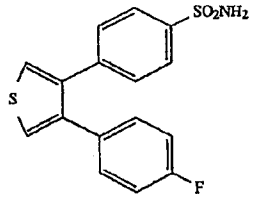
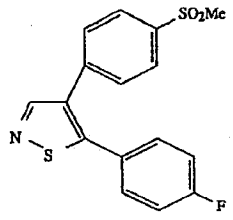
ED30(mg/kg)	STRUCTURE
1.40	
2.80 (in 1% methocel) 0.72	
0.43	
~3.00	
>3.00 3.00	
1.10	

TABLE IV-continued

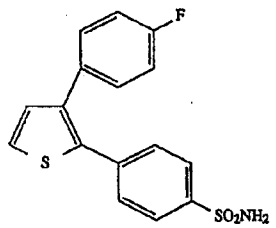
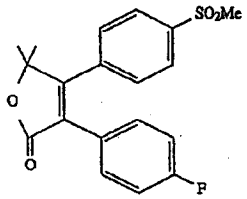
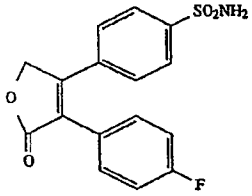
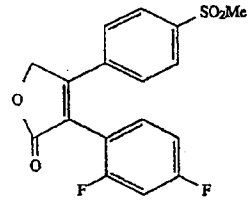
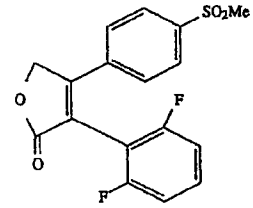
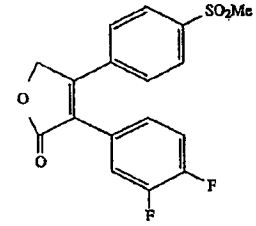
ED30(mg/kg)	STRUCTURE
>0.30	
0.42	
0.034	
2.03	
1.49	
0.35	

TABLE IV-continued

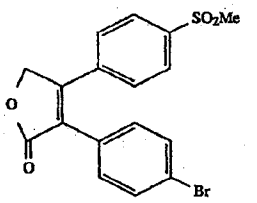
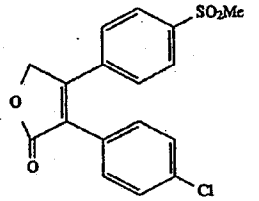
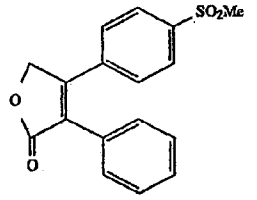
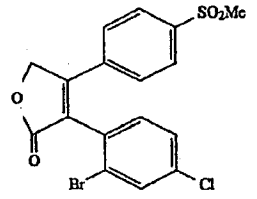
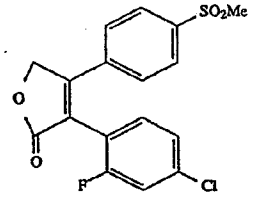
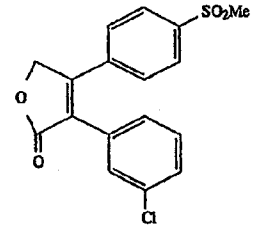
ED30(mg/kg)	STRUCTURE
0.33	
0.90	
0.38	
0.88	
0.47	
0.71	

TABLE IV-continued

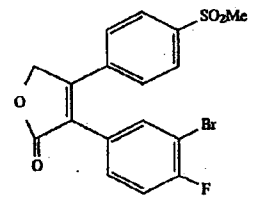
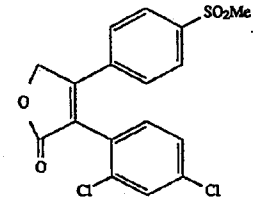
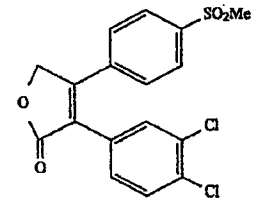
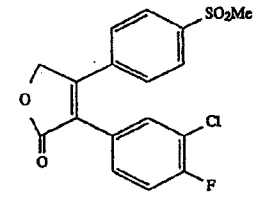
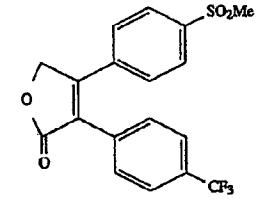
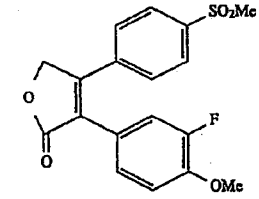
ED30(mg/kg)	STRUCTURE
~1.00	
1.85	
0.22 0.23	
0.43	
2.17	
0.81	

TABLE IV-continued

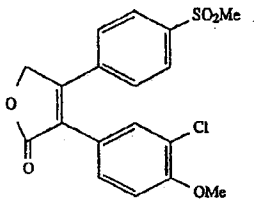
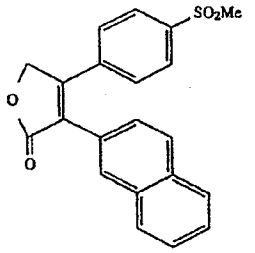
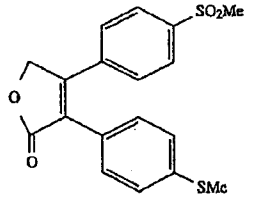
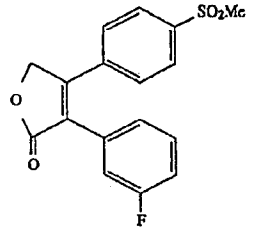
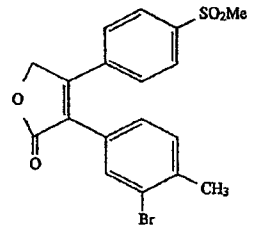
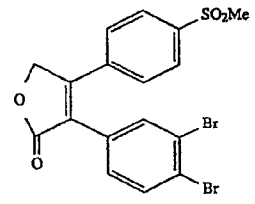
ED30(mg/kg)	STRUCTURE
0.68	
0.16	
~1.00	
0.33	
0.46	
0.76	

TABLE IV-continued

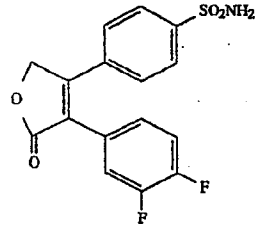
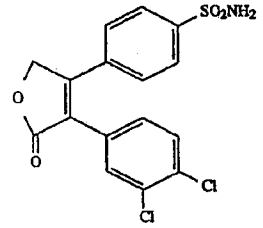
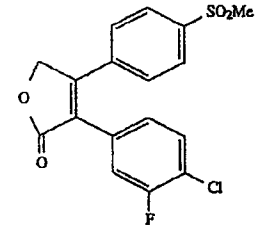
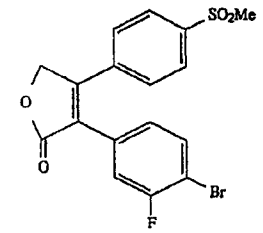
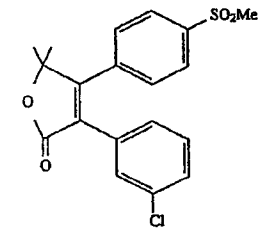
ED30(mg/kg)	STRUCTURE
0.48	
0.46	
0.26	
0.55	
0.25	

TABLE IV-continued

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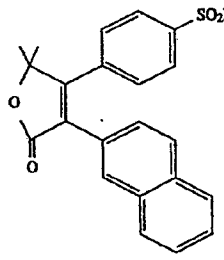
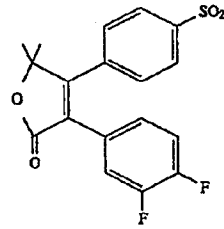
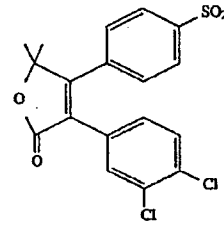
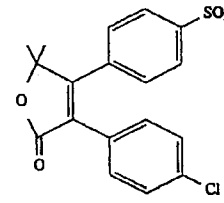
0.1–.3	
~0.10	
0.13	
0.07	

The invention will now be illustrated by the following non-limiting examples in which, unless stated otherwise:

(i) all operations were carried out at room or ambient temperature, that is, at a temperature in the range 18°–25° C.; evaporation of solvent was carded out using a rotary evaporator under reduced pressure (600–4000 pascals: 4.5–30 mm. Hg) with a bath temperature of up to 60° C.; the course of reactions was followed by thin layer chromatography (TLC) and reaction times are given for illustration only; melting points are uncorrected and 'd' indicates decomposition; the melting points given are those obtained for the materials prepared as described; polymorphism may result in isolation of materials with different melting points in some preparations; the structure and purity of all final products were assured by at least one of the following techniques: TLC, mass spectrometry, nuclear magnetic resonance (NMR) spectrometry or microanalytical data; yields are given for illustration only; when given, NMR data is in the form of delta (δ) values for major diagnostic protons, given in per million (ppm) relative to tetramethylsilane (TMS) as internal standard, determined at 300 MHz or 400 MHz using the indicated solvent; conventional abbreviations used for signal shape are: s. singlet; d. doublet; t. triplet; m. multipier; br. broad; etc.: in addition "Ar" signifies an aromatic signal; chemical symbols have their usual meanings; the following abbreviations have also been used v (volume), w (weight), b.p. (boiling point), m.p. (melting point), L (liter(s)), mL (milliliters), g (gram(s)), mg (milligrams(s)), mol (moles), mmol (millimoles), eq (equivalent(s)).

The following abbreviations have the indicated meanings:

Ac=acetyl
Bn=benzyl
DBU=1,8-diazabicyclo[5.4.0undec-7-ene
DIBAL=diisobutylaluminum hydride
DMAP=4-(dimethylamino)pyridine
DMF=N,N-dimethylformamide
Et_3N=triethylamine
LDA=lithium diisopropylamide
m-CPBA=metachloroperbenzoic acid
MMPP=monoperoxyphtalic acid
MPPM=monoperoxyphthalic acid, magnesium salt $6H_2O$
MS methanesulfonyl=mesyl=SO_2Me
MsO=methanesulfonate=mesylate
NSAID=non-steroidal anti-inflammatory drug
OXONE®=$2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$
PCC=pyridinium chlorochromate
PDC=pyridinium dichromate
Ph=phenyl
Phe=benzenediyl
Pye=pyridinediyl
r.t.=room temperature
rac.=racemic
SAM=aminosulfonyl or sulfonamide or SO_2NH_2
TBAF=tetra-n-butylammonium fluoride
Th=2- or 3-thienyl
TFAA=trifluoroacetic acid anhydride
THF=tetrahydrofuran
Thi=thiophenediyl
TLC=thin layer chromatography
TMS-CN=trimethylsilyl cyanide
Tz=1H (or 2H)-tetrazol-5-yl
C_3H_5=allyl

Alkyl Group Abbreviations

Me=methyl
Et=ethyl
n-Pr=normal propyl
i-Pr=isopropyl
n-Bu=normal butyl
i-Bu=isobutyl
s-Bu=secondary butyl
t-Bu=tertiary butyl
c-Pr=cyclopropyl
c-Bu=cyclobutyl
c-Pen=cyclopentyl
c-Hex=cyclohexyl

EXAMPLE 1

3-(4-Aminosulfonyl)phenyl)-2-(4-fluorophenyl)-5-(2-hydroxy-2-propyl)thiophene

Step 1: 1 -(4-Fluorophenyl)-2-(4-(methylthio)phenyl)ethanone

To 4-fluorobenzaldehyde (5.40 g) in 1,2-dichloroethane (43.50 mL) were added TMS-CN (4.32 g) and ZnI2 (44 mg). After 0.5 h at r.t., the solvent was removed in vacuo. To the resulting TMS cyanohydrin (9.20 g) in THF (42.0 mL) at −78° C. was added dropwise a solution of LDA 0.51M in THF (88.9 mL). After a period of 0.5 h, a THF solution (30.0 mL) of 4-(chloromethyl)thioanisole (9.93 g) was added dropwise over 0.5 h. After 18 h at +5° C., the resulting mixture was treated with TBAF (57.5 mL) followed by a 25% aqueous solution of NH_4OAc (100 mL) and extracted with EtOAc (2×150 mL). After evaporation, a 10:1 mixture of Et_2O and hexane (200 mL) was added to the crude ketone. After stirring for 10 h and filtration, the title product was obtained as a solid by filtration (2.40 g).

^1H NMR (CD_3COCD_3): δ2.45 (3H, s), 4.34 (2H, s), 7.19–7.29 (6H, m), 8.14 (2H, q).

Step 2: Cis,trans-3-chloro-3-(4-fluorophenyl)-2-(4-(methylthio)phenyl)propenal

To a solution of 1-(4-fluorophenyl)-2-(4-(methylthio)phenyl ethanone (2.50 g) in 1,2-dichloroethane (27.0 mL) were introduced the Viismeier reagent (Aldrich catalog, 1992–1993) 3.3M (11.6 mL) and DMAP (1.17 g). After a period of 4 h at 80° C., the reaction mixture was extracted with EtOAc and 25% aqueous solution of NH_4OAc. After evaporation in vacuo and drying for a few hours, the title product was used as such for the next step.

^1H NMR (CD_3COCD_3): δ2.40 and 2.48 (3H, 2s), 6.90–7.80 (8H, m), 9.55

Step 3: 5-(4-Fluorophenyl)-4-(4-(methylthio)phenyl)thiophene-2-carboxylic acid methyl ester

To a solution of cis,trans 3-chloro-3-(4-fluorophenyl)-2-(4(methylthio)phenyl)propenal (3.00 g) in pyridine (12.0 mL) were added methyl thioglycolate (1.16 mL) and Et_3N (4.09 mL). The resulting mixture was then heated at 80° C. for 2 h. After extraction with EtOAc and washing with 3N HCl, the title product was purified by flash chromatography (30% EtOAc in hexane) (2.00 g).

^1H NMR (CD_3COCD_3): δ2.48 (3H, s), 3.88 (3H, s), 7.11 (2H, t), 7.21 (4H, s), 7.37 (2H, q), 7.80 (1H, s).

Step 4: 5-(4-Fluorophenyl)-4-(4-(methylsulfinyl)phenyl)thiophene-2-carboxylic acid methyl ester

To a solution of 5-(4-fluorophenyl)-4-(4-(methylthio)phenyl)-thiophene-2-carboxylic acid methyl ester (5.60 g) in CH_2Cl_2 (84.0 mL) at 0° C. was added portionwise m-CPBA 50 to 60% (5.39 g). After TLC showed completion (50% EtOAc in hexane), the reaction mixture was extracted with saturated $NaHCO_3$, dried over Na_2SO_4, filtered and evaporated to dryness to provide the title compound as a white foam (5.00 g).

^1H NMR (CD_3COCD_3): δ2.75 (3H, s), 3.92 (3H, s), 7.15 (2H, t), 7.40 (2H, q), 7.52 (2H, d), 7.66 (2H, d), 7.90 (1H, s).

Step 5: 4-(4-(Aminosulfonyl)phenyl)-5-(4-fluorophenyl)thiophene-2-carboxylic acid methyl ester

5-(4-Fluorophenyl)-4-(4-(methylsulfinyl)phenyl)thiophene-2-carboxylic acid methyl ester (0.500 g) was dissolved in TFAA (10.0 mL) and refluxed for 0.5 h. The solvent was then removed in vacuo and the resulting residue was co-evaporated 10 times with a Et_3N-MeOH solution (1:1) (100.0 mL) to provide a viscous oil after pumping for a few hours. The oil was dissolved in HOAc (10.0 mL) and treated at + 10° C. with Cl_2 in HOAc (1.9M) (3.5 mL). After 20 min., the solvent was removed under reduced pressure and after pumping, THF (20.0 mL) was added to the resulting mass of product. After bubbling NH_3 through for a few minutes at 0° C., the reaction mixture was stirred for 0.5 h at r.t. After extraction with EtOAc −25% NH_4OAc solution and flash chromatography (30 to 40% EtOAc in hexane), the title product was obtained as a white solid (0.210 g).

^1H NMR (CD_3COCD_3): δ3.90 (3H, s), 6.55 (2H, bs), 7.13 (2H, t), 7.40 (2H, q), 7.46 (2H, d), 7.83 (2H, d), 7.90 (1H, s).

Step 6: 3-(4-Aminosulfonyl)phenyl)-2-(4-fluorophenyl)-5-(2-hydroxy-2-propyl)thiophene

To 4-(4-aminosulfonyl)phenyl)-5-(4-fluorophenyl)thiophene-2-carboxylic acid methyl ester (0.460 g) in THF (5.70 mL) at 0° C. was added MeMgBr (1 .4M) in toluene-THF solution (5.00 mL). The mixture was then stirred at r.t. for a few hours. The reaction was quenched by the addition of 25% NH_4OAc solution, extracted with EtOAc and dried over with Na_2SO_4. The title compound was purified by flash chromatography (40 to 50% EtOAc in hexane) (0.300 g).

^1H NMR (CD_3COCD_3): δ1.65 (6H, s), 4.52 (1H, s), 6.55 (2H, bs), 7.09 (3H, m), 7.34 (2H, dd), 7.30 (2H, m), 7.43 (2H, d), 7.82 (2H, d). Anal. calcd. for $C_{19}H_{18}FNO_3S_2$: C, 58.31; H, 4.60; N, 3.58. Found: C, 57.94; H, 4.66; N, 3.44

EXAMPLE 2

3-(4-(Aminosulfonyl)phenyl)-2-(4-fluorophenyl)thiophene

Step 1: 4-(4-(Aminosulfonyl)phenyl)-5-(4-fluorophenyl)thiophene-2-carboxylic acid

To a solution of 4-(4-(aminosulfonyl)phenyl)-5-(4-fluorophenyl)thiophene-2-carboxylic acid methyl ester (Example 1, Step 5) (0.210 g) in THF (2.0 mL) were added MeOH (1.0 mL), NaOH 1N (1.0 mL) and a few drops of NaOH 10N. The resulting mixture was heated at 45° C. for 2 h and the reaction was then partitioned between EtOAc and HCl (3N) to provide the title product as a white solid (0.200 g).

^1H NMR (CD_3COCD_3) δ6.60 (2H, s), 7.15 (2H, t), 7.35 (2H, q), 7.45 (2H, d), 7.82 (2H, d), 7.87 (1H, s).

Step 2: 3-(4-(Aminosulfonyl)phenyl)-2-(4-fluorophenyl)thiophene

To a solution of 3-(4-(aminosulfonyl)phenyl)-2-(4-fluorophenyl)thiophene-2-carboxylic acid (0.280 g) in quinoline (4.0 mL) was added Cu bronze (0.300 g). After 0.5 h at 180° C. under nitrogen, the reaction mixture was extracted with EtOAc and HCl 3N, dried over Na_2SO_4 and purified by flash chromatography (30% EtOAc in hexane) to give the title compound as a white solid (0.180 g).

^1H NMR (CD_3COCD_3): a 6.60 (2H, bs), 7.15 (2H, t), 7.29 (1H, d), 7.35 (2H, q), 7.45 (2H, d), 7.60 (1H, d), 7.83 (2H, d).

Anal. calcd for $C_{16}H_{12}FNO_2S_2$; C, 57.65; H, 3.60; N, 4.20.

Found: C, 57.62; H, 3.59; N, 4.15.

EXAMPLE 3

3 -(4-(Aminosulfonyl)phenyl)-2-(4-fluorophenyl)-5-(2-propyl)thiophene

^{1}H NMR (CD_3COCD_3) δ1.40 (6H, d), 3.25 (1H, septuplet), 6.58 (2H, bs), 7.05 (1H, s), 7.15 (2H, t), 7.32 (2H, dd), 7.46 (2H, d), 7.80 (2H, d).

Anal. calcd. for $C_{19}H_{18}FNO_2S_2$. C, 60.80; H, 4.80; N, 3.73.

Found: C, 60.59; H, 4.45; N, 3.60.

EXAMPLE 4

3-(4-(Aminosulfonyl)phenyl)-2-cyclohexylthiophene

^{1}H NMR ($CD_3)_2$)CO) δ1.24–1.40 (3H, m), 1.40–1.56 (2H, m), 1.65–1.85 (3H, m), 1.90–2.0 (2H, m), 3.18 (1H, m), 6.58 (2H, bs), 7.05 (1H, d), 7.37 (1H, d), 7.58 (2H, d), 7.97 (2H, d).

EXAMPLE 5

5-(4-Carboxyphenyl)-4-(4-(methylsulfonyl)phenyl) thiophene-2-carboxylic acid

Step 1: 4-(2-(4-Methylthiophenyl)-1-oxo-ethyl)benzoic acid methyl ester

To methyl 4-formylbenzoate (10.30 g) in 1,2-dichloroethane at r.t. were added TMS-CN (6.58 mL) and ZnI_2 (2.00 g), after 0.5 h at r.t., the solvent was removed in vacuo. To the resulting TMS cyanohyrin (5.00 g) in THF (22.0 mL) at −78° C. was added dropwise a solution of LDA 0.87 M in THF (26.2 mL). After a period of 0.5 h, a THF solution (10.0 mL) of 4-(chloromethyl)thioanisole was added dropwise over 0.5 h. The temperature was then brought slowly to −20° C. then to 5° C. for 2 h and TBAF 1M in THF (50.0 mL) was added. After the addition of 25% aqueous solution of NH_4OAc, the reaction mixture was extracted with EtOAc, dried over $NASO_4$, evaporated in vacuo and purified by flash chromatography (20 to 30% EtOAc in hexane) to afford the title compound as a white solid (7.00 g).

Step 2: 4-(1-Oxo-2-(4-(methylsulfonyl)phenyl)ethyl) benzoic acid methyl ester

To 7.10 g of 4-(2-(4-methylthiophenyl)-1-oxo-ethyl)benzoic acid methyl ester in MeOH (100 mL) was added oxone (21.0 g) in H_2O (20.0 mL) at 0° C. After a few hours at r.t., the reaction mixture was extracted with EtOAc and H_2O to afford after flash chromatography (50 to 100% EtOAc in hexane), the title product as a white solid (3.20 g).

^{1}H NMR (CD_3COCD_3) δ3.10 (3H, s), 3.95 (3H, s), 4.65 (2H, s), 7.60 (2H, d), 7.96 (2H, d), 8.20 (4H, q).

Step 3: Cis,trans 4-(1 -Chloro-3-oxo-2-(4-(methylsulfonyl)phenyl)- 1 -propenyl)benzoic acid methyl ester

To a solution of 4-(1-oxo-2-((4-methylsulfonyl)phenyl-)ethyl) benzoic acid (1.70 g) in 1,2-dichloroethane (15.0 mL) were added the Viismeier reagent 3.3 M (6.2 mL) and DMAP (0.624 g). The resulting mixture was heated at 80° C. for 4 h. The reaction mixture was then extracted with 25% aqueous solution of NH_4OAc and EtOAc. After drying over Na_2SO_4 and evaporation the title compound was obtained as an oil and used as such for the next step.

Step 4: 5-(4-(Methoxycarbonyl)phenyl)-4-(4-(methylsulfonyl)pheny)thiophene-2-carboxylic acid methyl ester

Prepared from 4-(1-chloro-3-oxo-2-(4-methylsulfonyl)phenyl)-1-propenyl)benzoic acid methyl ester as for Example 1, Step 3.

^{1}H NMR (CD_3COCD_3) δ3.13 (3H, s), 3.85 and 3.92 (6H, 25), 7.50 (2H, d), 7.55 (2H, d), 7.90 (2H, d), 7.92 (1H, s), 7.92 (2H, d).

Step 5: 5-(4-(Carboxyphenyl)-4-(4-(methyl)sulfonyl)phenyl)thiophene-2-carboxylic acid

Prepared from 5-(4-(methoxycarbonyl)phenyl)-4-(4(methyl)sulfonyl)phenyl) thiophene-2-carboxylic acid methyl ester as for Example 2, Step 1.

^{1}H NMR (CD_3COCD_3) δ3.15 (3H, s), 7.50 (2H, d), 7.62 (2H, d), 7.95 (2H, d), 7.98 (1H, s), 8.05 (2H, d).

Anal calcd. for $C_{19}H_{14}O_6S_2$·0.1 H_2O: C, 56.46; H, 3.51.

Found: C, 56.18; H, 3.51.

EXAMPLE 6

4-(4-Fluorophenyl)-2-methyl-5-(4-(methylsulfonyl)phenyl)thiazole

Step 1: 1-(4-Fluorophenyl)-2-(4-(methylsulfonyl)phenyl)ethanone

To 1-(4-Fluorophenyl)-2-(4-(methylthio)phenyl)ethanone of Example 1, Step 1 (17.9 g) in a solution of CH_2Cl_2-MeOH (272.0 mL/27.0 mL) at 0° C. was added MPPM (28.0 g). The cooling bath was then removed and the reaction mixture stirred at r.t. for 1 h. At 0° C., additional MPPM (28.0 g) was added and the reaction mixture kept for 1.5 h at r.t. The insoluble material was filtered followed by evaporation of the solvents, the residue was then extracted with CH_2Cl_2-$NaHCO_3$. After evaporation in vacuo, the resulting solid was washed with ether-hexane (1:1) and filtered to provide the title compound 16.8 g.

^{1}H NMR (CD_3COCD_3) δ3.13 (3H, s), 3.58 (2H, s), 7.29 (2H, t), 7.55 (2H, d), 7.88 (2H, d), 8.20 (2H, dd).

Step 2: 2-Bromo-1-(4-fluorophenyl)-2-(4-(methylsulfonyl)phenyl)ethanone

To 1-(4-Fluorophenyl)-2-(4-(methylsulfonyl)phenyl)ethanone (1.00 g) in CH_2Cl_2 containing $CHCl_3$ (1.0 mL) and CCl_4 (1.0 mL) was added bromine (0.614 g). After shining light for 1 h, the reaction was quenched with $Na_2S_2O_4$, extracted with CHl_2Cl_2, dried over Na_2SO_4 and evaporated to yield the title compound which was used as such for the next step (1.10 g).

^{1}H NMR (CD_3COCD_3) δ3.10 (3H, s), 7.05 (1H, s), 7.30 (2H, t), 7.87 (2H, d), 7.95 (2H, d), 8.25 (2H, dd).

Step 3: 4-(4-Fluorophenyl)-2-methyl-5-(4-(methylsulfonyl)phenyl)thiazole

To 2-bromo- 1 -(4-fluorophenyl)-2-(4-(methylsulfonyl)phenyl)ethanone (1.10 g) in ethanol (15.0 mL) were added thioacetamide (0.266 g) and pyridine (0.300 mL). After refluxing for 2 h, the reaction mixture was extracted with EtOAc, 25% NH_4OAc and purified by flash chromatography (50% EtOAc in hexane then 90% Et20 in hexane) to yield the title compound (0.320 g).

^{1}H NMR (CD_3COCD_3) δ2.72 (3H, s), 3.15 (3H, s), 7.09 (2H, t), 7.52 (2H, dd), 7.60 (2H, d), 7.92 (2H, d).

Anal. calcd. for $C_{17}H_{14}FNO_2S_2$: C, 58,78; H, 4.03; N, 4.03.

Found: C, 58.71, H, 4.17; N, 3.85.

EXAMPLE 7

2-(4-Fluorophenyl)-3-(4-(methylsulfonyl)phenyl)-2-cyclopenten-1-one

Step 1: 1-(4-Fluorophenyl)-5-hexen-2-one

To a suspension of 14.6 g (80 mmol) of $CdCl_2$ in 200 mL of ether cooled to 0° C. was added 115 mL of 1.3 M solution of 3-butene-1-magnesium bromide dropwise. The mixture was refluxed for 1 h and ether was then removed by distillation. Benzene (500 mL) was introduced, followed by a solution of 17.5 g (100 mmol) 4-fluorophenylacetyl chloride. After refluxing for 1 h, the reaction mixture was quenched with 200 mL of saturated aqueous NH_4Cl, 50 mL of 1 N HCl, and extracted with 200 mL of 1:1 hexane/EtOAC. The organic phase was dried over $MgSO_4$ and concentrated. The residue was purified by flash chromatography eluted with 4:1 hexanc/EtOAc to give 15 g of the title product.

^1H NMR ($CDCl_3$) δ2.40 (2H, t), 2.53 (2H, t), 3.63 (2H, s), 4.90–4.98 (2H, m), 5.67–5.78 (1H, m), 6.98 (2H, t), 7.13 (2H, m).

Step 2; 1-(4-Fluorophenyl)-5-oxo-2-pentanone

A solution of 14 g of 1-(4-fluorophenyl)-5-hexen-2-one in 200 mL of 3:1 CH_2Cl_2/MeOH was cooled to –78° C. and treated with excess ozone. The resulting mixture was treated with 15 g of triphenylphosphine and stirred at room temperature for 1 h. The reaction mixture was concentrated and flash chromatographed with 3:1 hexane/EtOAc to give 8 g of the title ketoaldehyde.

^1H NMR ($CDCl_3$) δ2.72 (4H, s), 3.71 (2H, s), 6.99 (2H, t), 7.14 (2H, m), 9.73 (1H, s).

Step 3: 2-(4-Fluorophenyl)-2-cyclopenten-1-one

A solution of 8 g of 1-(4-fluorophenyl)-5-oxo-2-pentanone in 300 mL of MeOH was treated with 2 g of NaOMe. The mixture was stirred for 2 h and then quenched with 5 mL of HOAc. The solvent was evaporated and the residue purified by flash chromatography, eluting with 3:1 hexane/EtOAc to give 7 g of the title product.

^1H NMR ($CDCl_3$) δ2.57 (2H, m), 2.68 (2H, m), 7.04 (2H, J=8.8 Hz, t), 7.67 (2H, J=8.8, 5.5 Hz, dd), 7.77 (1H, m).

Step 4: 1-(4-(Methylthio)phenyl)-2-(4-fluorophenyl)-2-cyclopenten-1-ol

To a solution of 3.86 g (19 mmol) of 4-bromothioanisole in 90 mL of Et_2O cooled at –78° C., was added 22 mL of 1.7 M solution of t-BuLi in pentane (38 mmol) dropwise. The reaction mixture was stirred for 15 min at –78° C. and a solution of 2.23 g of 2-(4-Fluorophenyl)-2-cyclopenten-1-one in 10 mL of Et_2O was added. After stirring for 15 min at –78° C., the reaction mixture was warmed to 0° C., and quenched with 50 mL of sat. NH_4Cl. The product was extracted with 100 mL EtOAc, dried over Na_2SO_4, and purified by flash chromatography, eluted with 4:1 hexane/EtOAc to give 3.4 g of the desired product.

^1H NMR ($CDCl_3$) δ2.12 (1H, s), 2.34 (2H, m), 2.44 (3H, s), 2.45–2.52 (1H, m), 2.56–2.65 (1H, m), 6.37 (1H, m), 6.84 (2H, J=8.7 Hz, t), 7.17 (2H, J=8.3 Hz, d), 7.24–7.33 (4H, m).

Step 5: 2-(4-Fluorophenyl)-3-(4-(methylthio)phenyl)-2-cyclopenten-1-one

To a suspension of PCC (4.5 g, 20.9 mmol) and 10 g of anhydrous 4Å molecular sieves in 150 mL of CH_2Cl_2 was added a solution of 2.2 g (7.3 mmol) of 1-(4-(methylthio)phenyl)-2-(4-fluorophenyl)-2-cyclopenten-1-ol in 20 mL CH_2Cl_2. The mixture was stirred for 1 h at r.t. and then diluted with 300 mL of Et_2O. After filtration and concentration, the residue was flash chromatographed with 2:1 hexane/EtOAc to give 1.5 g of the title product.

^1H NMR ($CDCl_3$) δ2.45 (3H, s), 2.68 (2H, m), 3.00 (2H, m), 7.02 (2H, J=8.6 Hz, t), 7.11 (2H, J=8.6 Hz, d), 7.15–7.23 (4H, m).

Step 6: 2-(4-Fluorophenyl)-3-(4-(methylsulfonyl)phenyl)-2-cyclopenten-1-one

To a solution of 50 mg (0.17 mmol) of 2-(4-Fluorophenyl)-3-(4-methylthio)phenyl)-2-cyclopenten -1-one in 8 mL of 10:1 CH_2Cl_2/MeOH was added 124 mg (0.2 mmol) of MPPM. The reaction mixture was stirred at room temperature for 2 h and then diluted with 10 mL of 1:1 hexane/EtOAc. After filtration and concentration, the residue was purified by flash chromatography eluted with 2:1 EtOAc/hexane to give 45 mg of the title product.

^1H NMR (acetone-d_6) δ2.67 (2H, m), 3.14 (3H, s), 3.16 (2H, m), 7.05–7.10 (2H, m), 7.20–7.25 (2H, m), 7.63 (2H, d), 7.93 (2H, d).

EXAMPLE 8

4-(4-(Methylsulfonyl)phenyl)-5-(4-fluorophenyl)-isothiazole

To a solution of 338 mg (1 mmol) of cis,trans 3-chloro-3-(4-fluorophenyl)-2-(4-(methylsulfonyl) phenyl)propenal in 5 mL of acetone was added 230 mg (3 mmol) of NH_4SCN. The reaction mixture was refluxed for 3 h, and then quenched with 20 mL of saturated $NaHCO_3$. The product was extracted with 100 mL of EtOAc, dried over Na_2SO_4, concentrated and purified by flash chromatography eluted with 3:2 hexane/EtOAc to give 250 mg of the title product.

^1H NMR ($CDCl_3$) δ8.57 (1H, s), 7.93 (3H, d), 7.50 (2H, d), 7.30 (2H, t), 7.08 (2H, t).

EXAMPLE 9

3-(4-Fluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

Step 1: 2-Bromo-1-(4-(methylsulfonyl)phenyl)ethanone

A solution of 197 g of 4-(Methylthio)acetophenone (ref: JACS, 1952, 74, p. 5475) in 700 mL of MeOH and 3500mL of CH_2Cl_2 was added 881 g of MMPP over a period of 30 min. After 3 h at room temperature the reaction mixture was filtered and the filtrate was washed with 2 L of saturated aqueous solution of $NaHCO_3$ and 1 L of brine. The aqueous phase was further extracted with 2 L of CH_2Cl_2. The combined extracts was dried over Na_2SO_4 concentrated to give 240 g of 4(methylsulfonyl)acetophenone as a white solid.

To a cooled (–5 ° C.) solution of 174 g of 4(methylsulfonyl)acetophenone in 2.5 L of $CHCl_3$ was added 20 mg of $AlCl_3$, followed by a solution of 40 mL of Br_2 in 300 mL $CHCl_3$. The reaction mixture was then treated with 1.5 L of water and the $CHCl_3$ was separated. The aqueous layer was extracted with 1 L of EtOAc. The combined extracts was dried over Na_2SO_4 and concentrated. The crude product was recystalized from 50/50 EtOAc/hexane to give 210 g of 2-bromo-1-(4-(methylsulfonyl)phenyl)ethanone as a white solid.

Step 2:

To the product of Step 1 (216 mg) dissolved in acetonitrile (4 mL) was added Et_3N (0.26 mL), followed by 4-fluorophenylacetic acid (102 mg). After 1.5 h at room temperature 0.23 mL of DBU was added. The reaction mixture was stirred for another 45 min and then treated with 5 mL of 1N HCl. The product was extracted with EtOAc, dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography (40% EtOAc in hexane) to yield 150 mg of the title compound as a solid.

^{1}H NMR (CD_3COCD_3) δ3.15 (3H, s), 5.36 (3H, s), 7.18 (2H, J=8.9 Hz, t), 7.46 (2H, m), 7.7 (2H, J=8.65 Hz, d), 7.97 (2H, J=8.68, d).

EXAMPLE 10

3-(4-Fluorophenyl)-4-(4-(aminosulfonyl)phenyl)-2-(2H)-furanone

^{1}H NMR (CD_3COCD_3) δ5.34 (2H, s), 6.67 (2H, bd), 7.18 (2H, m), 7.46 (2H, m), 7.61 (2H, m), 7.90 (2H, m). M.P. 187°–188 ° C. (d).

EXAMPLE 11

3-(4-Fluorophenyl)4-(4-(methylsulfonyl)phenyl)furan

Step 1:

Using the product of Example 10, (0.2 g) in THF (5 mL) and toluene (3 mL) was added slowly at –78° C. a solution of DIBAL (0.72 mL, 1M in toluene). After 15 min, the solution was warmed up to 0° C. for another 15 min. This mixture was then poured into a chilled aqueous solution of sodium potassium filtrate and EtOAc. The organic layer was stirred for 0.5 h with a few crystals of camphor sulfonic acid. This solution was then concentrated and purified by flash chromatography to yield the title compound.

^{1}H NMR ($CDCl_3$) _3.1 (3H, s), 7.02 (2H, J=8.9, t), 7.18 (2H, m), 7.4 (2H, J=8.8 Hz, d), 7.58 (1H, s), 7.68 (1H, s), 7.85 (2H, J=8.8 Hz, d)

EXAMPLE 12

5,5-Dimethyl-3-(4-fluorophenyl)-4-(4-methylsulfonylphenyl)-2-(5H)furanone

Step 1: Methyl 2-trimethylsilyloxyisobutyrate

To a solution of 1.2 mL (10.4 mmol) of methyl 2-hydroxyisobutyrate in 50 mL of CH_2Cl_2 were added 1.2 g (17.6 mmol) of imidazole and 2.1 mL (16.6 mmol) of TMSCl. The mixture was stirred at r.t. for 1.5 h and quenched with 20 mL of H_2O. The organic layer was dried over $MgSO_4$, concentrated and passed through a short plug of silica gel eluted with 9:1 hexane/EtOAc. Evaporation of solvent afforded 1.27 g of the title compound as a colorless oil.

^{1}H NMR (CD_3COCD_3) δ0.08 (9H, s), 1.38 (6H, s), 3.67 (3H, s).

Step 2: 2-Trimethylsilyloxy-4-(methylthio)isobutyrophenone

A solution of 204 mg(1.0 mmol) of 4-bromothioanisole in 2.5 mL of THF was cooled to –78° C. and treated with 0.42 mL of 2.5 M n-BuLi solution in hexane. After stirring at –78° C. for 1 h, a solution of 380 mg (2.0 mmol) of methyl 2-trimethylsilyloxyisobutyrate in 2 mL of THF was added. The mixture was stirred at –78° C. for 2 h and then quenched with NH_4OAc buffer. The product was extracted with EtOAc, dried over $MgSO_4$ and concentrated. The residue was purified by flash chromatography, eluting with 19:1 hexane/EtOAc to give 95 mg of the title product.

^{1}H NMR (CD_3COCD_3) δ0.05 (9H, s), 1.52 (6H, s), 2.53 (3H, s), 7.33 (2H, d), 8.12 (2H, d).

Step 3: 2-Hydroxy-4-(methylthio)isobutyrophenone

To a solution of 40 mg (0.14 mmol) of 2-trimethylsilyloxy-4-(methylthio)isobutyrophenone in 2 mL THF was added 0.2 mL of 1 M n-Bu_4NF in THF. The resulting mixture was stirred for 30 min and then quenched with 10 mL of NH_4OAc buffer. The product was extracted with EtOAc, dried over $MgSO_4$ and concentrated. The residue was purified by flash chromatography, eluting with 4:1 hexane/EtOAc to give 25 mg of the title product.

^{1}H NMR (CD_3COCD_3) δ1.50 (6H, s), 2.54 (3H, s), 4.68 (1H, s), 7.30 (2H, d), 8.15 (2H, d).

Step 4: 2-(4-Fluorophenylacetoxy)-4-(methylthio)isobutyrophenone

To a solution of 72 mg (0.34 mmol) 2-hydroxy-4-(methylthio)isobutyrophenone in 1.7 mL of CH_2Cl_2 were added 0.2 mL of pyridine and 140 mg (0.81 mmol) of 4-fluorophenylacetyl chloride. The mixture was stirred at room temperature overnight and then quenched with NH_4OAc buffer. The product was extracted with EtOAc, dried over $MgSO_4$ and concentrated. The crude product was purified by flash chromatography eluting with 8:1 hexane/EtOAc to give 95 mg of the title product.

^{1}H NMR (CD_3COCD_3) δ1.62 (3H, s), 1.67 (3H, s), 2.48 (3H, s), 3.79 (2H, s), 7.0–7.3 (6H, m), 7.78 (2H, d).

Step 5: 5,5-Dimethyl-3-(4-fluorophenyl-4-(4-methylthiophenyl)-2-(5H)-furanone

To a solution of 95 mg of 2-(4-fluorophenylacetoxy)-4-(methylthio)-isobutyrophenone in 4 mL of CH_2Cl_2 was added 0.2 mL of 1,8-diazabicyclo(5.4.0)undec-7-ene. The mixture was stirred for 4 h and diluted with NH_4OAc buffer. The product was extracted with EtOAc, dried over $MgSO_4$ and concentrated. The residue was purified by flash chromatography, eluting with 20:1 toluene/EtOAc to give 75 mg of the title product.

^{1}H NMR (CD_3COCD_3) δ1.58 (6H, s), 2.50 (3H, s), 7.03 (2H, dd), 7.25–7.35 (4H, m), 7.41 (2H, dd).

Step 5: 5-Dimethyl-3-(4-fluorophenyl)-4-(4-methylsulfonylphenyl)-2-(5H)-furanone

To a solution of 81 mg of 5,5-dimethyl-3-(4-fluorophenyl)-4-(4-methyl-thiophenyl)-2-oxo-2H -dihydrofuran in 1.8 mL of CH_2Cl_2 and 0.2 mL of MeOH was added 250 mg of MPPM. The reaction mixture was stirred at room temperature for 1 h and then quenched with aqueous $NaHCO_3$. The product was extracted with EtOAc, dried over $MgSO_4$ and concentrated. The crude product was purified by flash chromatography eluting with 1:1 hexane/EtOAc to give 73 mg of the title product.

^{1}H NMR (CD_3COCD_3) δ1.62 (6H, s), 3.15 (3H, s), 7.02 (2H, dd), 7.40 (2H, dd), 7.65 (2H, d), 8.03 (2H, d).

EXAMPLE 13

2-((4-aminosulfonyl)phenyl)-3-(4-fluorophenyl)thiophene

^{1}H NMR (CD_3COCD_3) δ6.60 (2H, bs), 7.12 (2H, t), 7.25 (1H, d), 7.35 (2H, m), 7.45 (2H, d), 7.65 (1H, d), 7.85 (2H, d).

Analysis calculated for $C_{16}H_{12}FNS_2O_2$ C, 57.65; H, 3.60; N, 4.20

Found: C, 57.55; H, 3.79; N, 4.03

EXAMPLE 14

3-(4-(Trifluoroacetylaminosulfonyl)phenyl)-2-(4-fluorophenyl)thiophene

^{1}H NMR (300 MHz, CD_3COCD_3) δ7.15 (2H, t), 7.30 (3H, m), 7.45 (2H, d), 7.65 (1H, d), 7.95 (2H, d).

EXAMPLE 15

3-(2,4-Difluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

Analysis calculated for $C_{17}H_{12}F_2O_4S$ C, 58.28; H, 3.45; S, 9.15

Found: C, 58.27; H, 3.50; S, 9.27

EXAMPLE 16

3 -(3,4-Difluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

To a solution of 3,4-difluorophenylacetic acid (ALDRICH CHEMICAL) (10 g) and 2-bromo-1-(4-(methylsulfonyl)phenyl)ethanone Example 9, Step 1) (17.3 g) in acetonitrile (200 mL) at room temperature was added slowly triethylamine (20.2 mL). After 1 h at room temperature, the mixture was cooled in an ice bath and treated with 17.4 mL of DBU. After 2 h at 0° C., the mixture was treated with 200 mL of 1N HCl and the product was extracted with EtOAc, dried over Na_2SO_4 and concentrated. The residue was applied on top of a silica gel plug (sintered glass funnel) eluted with 75% EtOAc/hexane, giving after evaporation of the solvent and swish in ethyl acetate, 10 g of the title compound.

Analysis calculated for $C_{17}H_{12}F_2O_4S$ C, 58.28; H, 3.45; S, 9.15

Found: C, 58.02; H, 3.51; S, 9.35

EXAMPLE 17

3-(2,6-Difluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

Analysis calculated for $C_{17}H_{12}F_2O_4S$ C, 58.28; H, 3.45; S, 9.15

Found: C, 58.18; H, 3.50; S, 9.44

EXAMPLE 18

3-(2,5-Difluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

Analysis calculated for $C_{17}H_{12}F_2O_4S$ C, 58.28; H, 3.45; S, 9.15

Found: C, 58.89; H, 3.51; S, 9.11

EXAMPLE 19

3-(3,5-Difluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

Analysis calculated for $C_{17}H_{12}F_2O_4S$ C, 58.28; H, 3.45; S, 9.15

Found: C, 58.27; H, 3.62; S, 9.32

EXAMPLE 20

3-(4-Bromophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

Analysis calculated for $C_{17}H_{13}BrO_4S$ C, 51.94; H, 3.33; S, 8.16

Found: C, 51.76; H, 3.42; S, 8.21

EXAMPLE 21

3,(4-Chlorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

^{1}H NMR (300 MHz, $CDCl_3$) δ7.93 (2H, d), 7.49 (2H, d), 7.35 (4H, m), 5.16 (2H, s), 3.06 (3H, s)

EXAMPLE 22

3-(4-Methoxyphenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

Analysis calculated for $C_{18}H_{16}O_5S$ C, 62.78 H, 4.68; S, 9.31

Found: C, 62.75; H, 4.72; S, 9.39

EXAMPLE 23

3-(Phenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

To a solution of phenylacetic acid (27.4 g, 201 mmol) and 2-bromo-1-(4-(methylsulfonyl) phenyl)ethanone (Example 9, Step 1) (60 g, 216 mmol, 1.075 eq.) in acetonitrile (630 mL) at 25° C. was added slowly triethylamine (30.8 mL, 1.1 eq.). The mixture was stirred for 20 min. at room temperature and then cooled in an ice bath. DBU (60.1 mL, 3 eq.) was slowly added. After stirring for 20 min. in the ice bath, the reaction was complete and the mixture was acidified with 1N HCl (color changes from dark brown to yellow). Then 2.4 L of ice and water were added, stirred for a few minutes, then the precipitate was filtered and rinsed with water (giving 64 g of crude wet product). The solid was dissolved in 750 mL of dichloromethane (dried over $MgSO_4$, filtered) and 300 g of silica gel was added. The solvent was evaporated to near dryness (silica gel a bit sticky) and the residue was applied on top of a silica gel plug (sintered glass funnel) eluted with 10% EtOAc/CH_2Cl_2, giving after evaporation of the solvent and swish in ethyl acetate, 36.6 g (58%) of the title compound.

Analysis calculated for $C_{17}H_{14}O_4S$ C, 64.95; H, 4.49; S, 10.20

Found: C, 64.63; H, 4.65; S, 10.44

EXAMPLE 24

3-(2-Chlorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

Analysis calculated for $C_{17}H_{13}ClO_4S$ C, 58.54; H, 3.76; S, 9.19

Found: C, 58.59; H, 3.80; S, 9.37

EXAMPLE 25

3-(2-Bromo-4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

Analysis calculated for $C_{17}H_{12}BrFO_4S$ C, 49.75; H, 2.93

Found: C, 49.75; H, 3.01

EXAMPLE 26

3-(2-Bromo-4-Chlorophenyl)-4-(4-(methylsulfonyl) phenyl)-2-(5H)-furanone

^{1}H NMR (300 MHz, acetone-d_6) δ7.95 (2H, d), 7.85 (1H, d), 7.63 (2H, dd), 7.55 (1H, dd), 7.45 (1H, d), 5.50 (2H, s), 3.15 (3H, s)

EXAMPLE 27

3-(4-Chloro-2-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

^{1}H NMR (300 MHz, acetone-d_6) δ8.0 (2H, d), 7.70 (2H, d), 7.50–7.30 (3H, m), 5.35 (2h, s), 3.15 (3H, s)

EXAMPLE 28

3 -(3-Bromo-4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)

Analysis calculated for $C_{17}H_{12}BrFO_4S$ C, 49.75; H, 2.93
Found: C, 49.44; H, 2.98

EXAMPLE 29

3-(3-Chlorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

Analysis calculated for $C_{17}H_{13}ClO_4S$ C, 58.54; H, 3.76
Found: C, 58.29; H, 3.76

EXAMPLE 30

3-(2-Chloro-4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

Analysis calculated for $C_{17}H_{12}ClFO_4S$ C, 55.67; H, 3.30
Found: C, 55.67; H, 3.26

EXAMPLE 31

3-(2,4-Dichlorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

Analysis calculated for $C_{17}H_{12}Cl_2O_4S$ C, 53.28; H, 3.16; S, 8.37
Found: C, 52.89; H, 3.23; S, 8.58

EXAMPLE 32

3-(3,4-Dichlorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

Analysis calculated for $C_{17}H_{12}Cl_2O_4S$ C, 53.28; H, 3.16; S, 8.37
Found: C, 53.07; H, 3.32; S, 8.51

EXAMPLE 33

3-(2,6-Dichlorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

Analysis calculated for $C_{17}H_{12}Cl_2O_4S$ C, 53.28; H, 3.16; S, 8.37
Found: C, 52.99; H, 3.22; S, 8.54

EXAMPLE 34

3-(3-Chloro-4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

^{1}H NMR (300 MHz, acetone-d_6) δ8.0 (2H, d), 7.70 (2H, d), 7.60 (1H, d), 7.25–7.40 (2H, m), 5.35 (2H, s), 3.15 (3H, s)

EXAMPLE 35

3-(4-Trifluoromethylphenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

^{1}H NMR (CD_3COCD_3) δ8.10 (2H, d), 7.82–7.93 (4H, m), 7.75 (2H, d), 5.55 (2H, s), 3.30 (3H, s)

EXAMPLE 36

3-(3-Fluoro-4-methoxyphenyl)-4-(4-(methylsulfonyl) phenyl)-2-(5 H)-furanone

Analysis calculated for $C_{18}H_{15}OF_5S$ C, 59.66; H, 4.17
Found: C, 59.92; H, 4.37

EXAMPLE 37

3-(3-Chloro-4-methoxyphenyl)-4-(4-(methylsulfonyl) phenyl-2-(5H)-furanone

Analysis calculated for $C_{18}H_{15}ClO_5S$ C, 57.07; H, 3.99
Found: C, 57.29; H, 4.15

EXAMPLE 38

3-(3-Bromo-4-methoxyphenyl)-4-(4-(methylsulfonyl) phenyl)-2-(5H)-furanone

Analysis calculated for $C_{18}H_{15}BrO_5S$ C, 51.08; H, 3.57
Found: C, 51.38; H, 3.62

EXAMPLE 39

3-(2-Fluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

Analysis calculated for $C_{17}H_{13}FO_4S$ C, 61.44; H, 3.94
Found: C, 61.13; H, 3.85

EXAMPLE 40

3-(4-Methylthiophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

^{1}H NMR (300 MHz, acetone-d_6) δ8.0 (2H, d), 7.70 (2H, d), 7.35 (2H, d), 7.25 (2H, d), 5.35 (2H, s), 3.15 (3H, s), 2.55 (3H, s)

EXAMPLE 41

3-(3-Fluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

^{1}H NMR (300 MHz, $CDCl_3$) δ7.93 (2H, d), 7.49 (2H, d), 7.35 (1H, m), 7.12 (3H, m), 5.18 (2H, s), 3.06 (3H, s)

EXAMPLE 42

3-(2-Chloro-6-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

^{1}H NMR (300 MHz, acetone-d_6), δ8.0 (2H, d), 7.70 (2H, d), 7.55–7.65 (1H, m), 7.40 (1H, d), 7.30 (1H, m), 5.60 (2H, s), 3.15 (3H, s)

EXAMPLE 43

3-(3-Bromo-4-methylphenyl)-4-(4-(methylsulfonyl) phenyl)-2-(5-H)-furanone

Analysis calculated for $C_{18}H_{15}BrO_4S$ C, 53.08; H, 3.71
Found: C, 53.06; H, 3.83

EXAMPLE 44

3-(4-Bromo-2-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

Analysis calculated for $C_{17}H_{12}BrFO_4S$ C, 49.65; H, 2.94
Found: C, 49.76; H, 3.00

EXAMPLE 45

3-(3,4-Dibromophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

^{1}H NMR (300 MHz, acetone-d_6) δ8.0 (2H, d), 7.80 (1H, d), 7.75 (3H, m), 7.25 (1H, d), 5.35 (2H, s), 3.15 (sH, s)

EXAMPLE 46

3-(4-Chloro-3-fluorophenyl)-4-(4-(methylsulfonyl) phenyl)-2-(5H)-furanone

Analysis calculated for $C_{17}H_{12}ClFO_4S$ C, 55.67; H, 3.30
Found: C, 55.45; H, 3.30

EXAMPLE 47

3-(4-Bromo-3-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

Analysis calculated for $C_{17}H_{12}BrFO_4S$ C, 49.66; H, 2.94; S, 7.80
Found: C, 49.79; H, 3.01; S, 7.51

EXAMPLE 48

3-(4-Bromo-2-chlorophenyl)-4-(4-(methylsulfonyl) phenyl)-2-(5H)-furanone

Analysis calculated for $C_{17}H_{12}BrClO_4S$ C, 47.74; H, 2.83; S, 7.50
Found: C, 47.92; H, 2.84; S, 7.42

EXAMPLE 49

3-(2-Naphthyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

Analysis calculated for $C_{21}H_{16}O_4S$ C, 69.22; H, 4.43
Found: C, 69.22; H, 4.46

EXAMPLE 50

3-(7-Quinolinyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone

Analysis calculated for $C_{20}H_{15}NO_4S$ C, 65.74; H, 4.14; N, 3.83
Found: C, 65.34; H, 4.40; N, 3.80
M.S. (DCI, CH_4) calculated for M^+, 365 Found for M^++1, 366

EXAMPLE 51

3-(3,4-Dichlorophenyl)-4-(4-(aminosulfonyl)phenyl)-2-(2H)-furanone

^{1}H NMR (400 MHz, CD_3COCD_3) δ7.92 (2H, dd), 7,64 (3H, din), 7.60 (1H, dd), 7.32 (1H, dd), 6.70 (1H, bs), 5.38 (2H, s)

EXAMPLE 52

3-(
3,4-Difluorophenyl)-4-(4-(aminosulfonyl)phenyl)-2-(2H)-furanone

^{1}H NMR (400 MHz, CD_3COCD_3) δ7.92 (2H, dd), 7,64 (2H, dd), 7.30–7.45 (2H, m), 7.22 (1H, m), 6.68 (2H, bs), 5.37 (2H, s)

EXAMPLE 53

3-(3-Chloro-4-methoxyphenyl)-4-(4-(aminosulfonyl) phenyl)-2-(2H)-furanone

Analysis calculated for $C_{17}H_{14}ClNO_5S$ C, 53.76; H, 3.72, N, 3.69
Found: C, 53.32; H, 3.84, N, 3.59
M.S. (DCI, CH_4) calculated for M^+, 379 Found for M^++1, 380

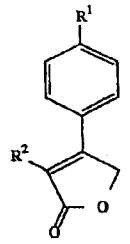
EXAMPLE 54

3-(3-Bromo-4-methoxyphenyl)-4-(4-(aminosulfonyl) phenyl)-2-(2H)-furanone

Analysis calculated for $C_{17}H_{14}BrNO_5S$ C, 48.13; H, 3.33, N, 3.30
Found: C, 48.26; H, 3.40, N, 3.28
M.S. (DCI, CH_4) calculated for M^+, 423 Found for M^++1, 424

What is claimed is:

1. A compound of the formula XXXIII



XXXIII

or a pharmaceutically acceptable salt thereof wherein:

R^1 is selected from the group consisting of

(a) $S(O)_2CH_3$,

(b) $S(O)_2NH_2$,

(c) $S(O)_2NHC(O)CF_3$,

(d) $S(O)(NH)CH_3$,

(e) $S(O)(NH)NH_2$,

(f) $S(O)(NH)NHC(O)CF_3$,

(g) $P(O)(CH_3)OH$, and

(h) $P(O)(CH_3)NH_2$,

R^2 is selected from the group consisting of

(a) C_{1-6}alkyl,

(b) C_3, C_4, C_5, C_6, and C_7, cycloalkyl,

(c) mono-, di- or tri-substituted phenyl wherein the substituent is selected from the group consisting of

(1) hydrogen,

(2) halo,

(3) C_{1-6}alkoxy,

(4) C_{1-6}alkylthio,

(5) CN,

(6) CF_3,

(7) C_{1-6}alkyl,

(8) N_3,

(9) $—CO_2H$,

(10) $—CO_2—C_{1-4}$alkyl,

(11) $—C(R^5)(R^6)—OH$,

(12) $—C(R^5)(R^6)—O—C_{1-4}$alkyl, and

(13) $—C_{1-6}$alkyl$—CO_2—R^5$;

(d) mono-, di- or tri-substituted heteroaryl wherein the heteroaryl is a monocyclic aromatic ring of 5 atoms, said ring having one hetero atom which is S, O, or N, and optionally 1, 2, or 3 additional N atoms; or

the heteroaryl is a monocyclic ring of 6 atoms, said ring having one hetero atom which is N, and optionally 1, 2 or 3 additional N atoms; said substituents are selected from the group consisting of

(1) hydrogen,

(2) halo, including fluoro, chloro, bromo and iodo,

(3) C_{1-6}alkyl,

(4) C_{1-6}alkoxy,

(5) C_{1-6}alkylthio,

(6) CN,

(7) CF_3,

(8) N_3,

(9) $—C(R^5)(R^6)—OH$,

(10) $—C(R^5)(R^6)—O—C_{1-4}$alkyl;

R^5 and R^6 are each independently selected from the group consisting of

(a) hydrogen,

(b) C_{1-6}alkyl,

or R^5 and R^6 together with the carbon to which they are attached form a monocyclic saturated carbon ring of 3, 4, 5, 6 or 7 atoms.

2. A compound according to claim 1 wherein

R^1 is selected from the group consisting of

(a) $S(O)_2CH_3$,

(b) $S(O)_2NH_2$,

(c) $S(O)_2NHC(O)CF_3$,

(d) $S(O)NHCH_3$,

(e) $S(O)NHNH_2$, and

(f) $S(O)NHNHC(O)CF_3$;

R^2 is selected from the group consisting of

(a) C_{1-4}alkyl,

(b) C_3, C_4, C_5, C_6, and C_7, cycloalkyl,

(c) mono- or di-substituted phenyl wherein the substituent is selected from the group consisting of

(1) hydrogen,

(2) fluoro, chloro, and bromo,

(3) C_{1-4}alkoxy,

(4) C_{1-4}alkylthio,

(5) CN,

(6) CF_3,

(7) C_{1-4}alkyl,

(8) N_3,

(9) $—CO_2H$,

(10) $—CO_2—C_{1-3}$alkyl,

(11) $—C(R^5)(R^6)—OH$, and

(12) $—C(R^5)(R^6)—O—C_{1-3}$alkyl.

3. A compound according to claim 2 wherein R^2 is selected from the group consisting of

(a) cyclohexyl, and

(b) mono- or di-substituted phenyl, and wherein the substitutents are selected from the group consisting of

(1) hydrogen,

(2) halo,

(3) C_{1-4}alkoxy,

(4) C_{1-4}alkylthio,

(5) CN,

(6) CF_3,

(7) C_{1-4}alkyl,

(8) N_3, and

(9) $—C(R^5)(R^6)—OH$;

R^5 and R^6 are each independently selected from the group consisting of

(a) hydrogen,

(b) methyl or ethyl, or R^5 and R^6 together with the carbon to which they are attached form a saturated carbon ring of 4, 5 or 6 atoms.

4. A compound according to claim 3 wherein

R^1 is selected from the group consisting of

(a) $S(O)_2CH_3$,

(b) $S(O)_2NH_2$,

(c) $S(O)NHCH_3$, and

(d) $S(O)NHNH_2$;

R^2 is selected from the group consisting of mono or di-substituted phenyl wherein the substitutents are selected from the group consisting of

(1) hydrogen,

(2) halo, selected from the group consisting of fluoro, chloro and bromo,

(3) C_{1-3}alkoxy,
(4) C_{1-3}alkylthio,
(5) CN, and
(6) C_{1-3}alkyl.

5. A compound according to claim 4 whercin R^1 is selected from the group consisting of
(a) $S(O)_2CH_3$,
(b) $S(O)_2NH_2$,
(c) $S(O)NHCH_3$, and
(d) $S(O)NHNH_2$;
R^2 is mono or di-substituted phenyl wherein the substitutents are selected from the group consisting of
(1) hydrogen,
(2) halo, selected from the group consisting of fluoro, chloro and bromo,
(3) methoxy, and
(4) methyl.

6. A compound according to claim 5 wherein R^1 is selected from the group consisting of
(a) $S(O)_2CH_3$, and
(b) $S(O)_2NH_2$,
R^2 is mono or di-substituted phenyl wherein the substitutents are selected from the group consisting of
(1) hydrogen,
(2) halo, selected from the group consisting of fluoro, chloro and bromo.

7. A compound according to claim 2 wherein R^2 is a mono- or di-substituted heteroaryl wherein heteroaryl is selected from the group consisting of
(1) furanyl,
(2) diazinyl, triazinyl, tetrazinyl,
(3) imidazolyl,
(4) isooxazolyl,
(5) isothiazolyl,
(6) oxadiazolyl,
(7) oxazolyl,
(8) pyrazolyl,
(9) pyrrolyl,
(10) thiadiazolyl,
(11) thiazolyl,
(12) thienyl,
(13) triazolyl, and
(14) tetrazolyl,
wherein the substitutents are selected from the group consisting of
(a) hydrogen,
(b) fluoro or chloro,
(c) C_{1-3}alkoxy,
(d) C_{1-6}alkylthio,
(e) CN,
(5) CF_3,
(6) C_{1-3}alkyl,
(7) $—C(R^5)(R^6)—OH$;
(8) $—C(R^5)(R^6)—O—C_{1-4}$alkyl.

8. A compound according to claim 7 wherein R^2 is a mono- or di-substituted heteroaryl wherein heteroaryl is selected from the group consisting of
(1) 2-furanyl,
(2) 3-furanyl,
(3) 2-thienyl,
(4) 3-thienyl,
(5) 3-isoxazolyl,
(6) 4-isoxazolyl,
(7) 5-isoxazolyl,
(8) 3-isothiazolyl,
(9) 4-isothiazolyl,
(10) 5-isothiazolyl,
(11) 2-oxazolyl,
(12) 4-oxazolyl,
(13) 5-oxazolyl,
(14) 2-thiazolyl,
(15) 4-thiazolyl,
(16) 5-thiazolyl,
(17) 1,2,3-thiadiazol-4-yl,
(18) 1,2,3-thiadiazol-5-yl,
(19) 1,2,4-thiadiazol-3-yl,
(20) 1,2,4-thiadiazol-5-yl,
(21) 1,3,4-thiadiazol-2-yl,
(22) 1,2,5-thiadiazol-3-yl,
(23) 1,2,3-oxadiazol-4-yl,
(24) 1,2,3-oxadiazol-5-yl,
(25) 1,2,4-oxadiazol-3-yl,
(26) 1,2,4-oxadiazol-5-yl,
(27) 1,3,4-oxadiazol-2-yl,
(28) 1,2,5-oxadiazol-3-yl,
(29) pyrazol-4-yl,
(30) pyrazol-5-yl,
(31) 1,2,3-triazol-4-yl,
(32) 1,2,3-triazol-5-yl,
(33) 1,2,4-triazol-3-yl,
(34) 1,2,4-triazol-5-yl,
(35) 1,2-diazinyl,
(36) 1,3-diazinyl,
(37) 1,4-diazinyl,
(38) 1,2,3,4-tetrazin-5-yl,
(39) 1,2,4,5-tetrazin-4-yl,
(40) 1,3,4,5-tetrazin-2-yl,and
(41) 1,2,3,5-tetrazin-4-yl.

9. A compound according to claim 8 wherein the heteroaryl is selected from the group consisting of
(1) 3-isoxazolyl,
(2) 4-isoxazolyl,
(3) 5-isoxazolyl,
(4) 3-isothiazolyl,
(5) 4-isothiazolyl,
(6) 5-isothiazolyl,
(7) 2-oxazolyl,
(8) 4-oxazolyl,
(9) 5-oxazolyl,
(10) 2-thiazolyl,
(11) 4-thiazolyl,
(12) 5-thiazolyl,
(13) 1,2,3-thiadiazol-4-yl,
(14) 1,2,3-thiadiazol-5-yl,
(15) 1,2,4-thiadiazol-3-yl,
(16) 1,2,4-thiadiazol-5-yl,
(17) 1,3,4-thiadiazol-2-yl,
(18) 1,2,5-thiadiazol-3-yl,

(19) 1,2,3-oxadiazol-4-yl,
(20) 1,2,3-oxadiazol-5-yl,
(21) 1,2,4-oxadiazol-3-yl,
(22) 1,2,4-oxadiazol-5-yl,
(23) 1,3,4-oxadiazol-2-yl,
(24) 1,2,5-oxadiazol-3-yl,
(25) 1,2-diazinyl,
(26) 1,3-diazinyl, and
(27) 1,4-diazinyl.

10. A compound according to claim **9** wherein the heteroaryl is selected from the group consisting of

(1) 3-isothiazolyl,
(2) 4-isothiazolyl,
(3) 5-isothiazolyl,
(4) 2-oxazolyl,
(5) 4-oxazolyl,
(6) 5-oxazolyl,
(7) 2-thiazolyl,
(8) 4-thiazolyl,
(9) 5-thiazolyl,
(10) 1,2-diazinyl,
(11) 1,3-diazinyl, and
(12) 1,4-diazinyl, and

wherein the substitutents are selected from the group consisting of

(1) hydrogen,
(2) fluoro or chloro,
(3) C_{1-3}alkoxy,
(4) C_{1-3}alkylthio,
(5) CN,
(6) C_{1-3}alkyl, and
(7) $—C(R^5)(R^6)—OH$,

wherein R^5 and R^6 are each independently hydrogen, methyl or ethyl.

11. A compound according to claim **10** wherein R^1 is selected from the group consisting of

(a) $S(O)_2CH_3$,
(b) $S(O)_2NH_2$,
(c) $S(O)NHCH_3$, and
(d) $S(O)NHNH_2$.

12. A compound according to claim **11** wherein the hetereooaryl is selected from the group consisting of

(1) 3-isothiazolyl,
(2) 4-isothiazolyl,
(3) 5-isothiazolyl,
(4) 2-oxazolyl,
(5) 4-oxazolyl,
(6) 5-oxazolyl,
(7) 2-thiazolyl,
(8) 4-thiazolyl,
(9) 5-thiazolyl,
(10) 1,2-diazinyl,
(11) 1,3-diazinyl, and
(12) 1,4-diazinyl, and

wherein the substitutents are selected from the group consisting of

(1) hydrogen,
(2) fluoro or chloro,
(3) methoxy,
(4) methylthio,
(5) CF_3,
(6) methyl.

13. A compound according to claim **1** selected from

(1) 3-(3-Fluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone,
(2) 3-(3,4-Difluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2(5H)-furanone,
(3) 3-(3,4-trichlorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone,
(4) 3-phenyl-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone.

14. A compound which is

3-(3,4-Difluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2(5H)-furanone,

(b) 3-phenyl-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone, or a pharmaceutically acceptable salt thereof.

15. A compound according to claim **1** selected from

(1) 3-(4-Fluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone,
(2) 3-(4-Fluorophenyl)-4-(4-(aminosulfonyl)phenyl)-2-(5H)-furanone,
(3) 3-(2,4-Difluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone,
(4) 3-(3,4-Difluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone,
(5) 3-(2,6-Difluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone,
(6) 3-(2,5-Difluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone,
(7) 3-(3,5-Difluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone,
(8) 3-(4-Bromophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone,
(9) 3-(4-Chlorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone,
(10) 3-(4-Methoxyphenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone,
(11) 3-(Phenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone,
(12) 3-(2-Chlorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone,
(13) 3-(2-Bromo-4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)2-(5H)-furanone,
(14) 3-(2-Bromo-4-Chlorophenyl)-4-(4-(methylsulfonyl)phenyl)2-(5H)-furanone,
(15) 3-(4-Chloro-2-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)2-(5H)-furanone,
(16) 3-(3-Bromo-4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)2-(5H)-furanone,
(17) 3-(3-Chlorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone,
(18) 3-(2-Chloro-4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)2-(5H)-furanone,
(19) 3-(2,4-Dichlorophenyl)-4-(4-(methylsulfonyl)phenyl)-2(5H)-furanone,
(20) 3-(3,4-Dichlorophenyl)-4-(4-(methylsulfonyl)phenyl)-2(5H)-furanone,
(21) 3-(2,6-Dichlorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone,

(22) 3-(3-Chloro-4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)2-(5H)-furanone,

(23) 3-(4-Trifluoromethylphenyl)-4-(4-(methylsulfonyl)phenyl)2-(5H)-furanone,

(24) 3-(3-Fluoro-4-methoxyphenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone,

(25) 3-(3-Chloro-4-methoxyphenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone,

(26) 3-(3-Fluoro-4-methoxyphenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone,

(27) 3-(2-Fluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone,

(28) 3-(4-Methylthiophenyl)-4-(4-(methylsulfonyl)phenyl)-2(5H)-furanone,

(29) 3-(3-Fluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone,

(30) 3-(2-Chloro-6-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone,

(31) 3-(3-Bromo-4-methylphenyl)-4-(4-(methylsulfonyl)phenyl)2-(5H)-furanone,

(32) 3-(4-Bromo-2-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)2-(5H)-furanone,

(33) 3-(3,4-Dibromophenyl)-4-(4-(methylsulfonyl)phenyl)-2(5H)-furanone,

(34) 3-(4-Chloro-3-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)2-(5H)-furanone,

(35) 3-(4-Bromo-3-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)2-(5H)-furanone, and

(36) 3-(4-Bromo-2-chlorophenyl)-4-(4-(methylsulfonyl)phenyl)2-(5H)-furanone.

16. A compound according to claim 1 selected from

(1) 3-(3,4-Dichlorophenyl)-4-(4-(aminosulfonyl)phenyl)-2-(5H)-furanone,

(2) 3-(3,4-Difluorophenyl)-4-(4-(aminosulfonyl)phenyl)-2-(5H)-furanone,

(3) 3-(3-Chloro-4-methoxyphenyl)-4-(4-(aminosulfonyl)phenyl)2-(5H)-furanone, and

(4) 3-(3-Bromo-4-methoxyphenyl)-4-(4-(aminosulfonyl)phenyl)2-(5H)-furanone.

17. A compound which is 3-phenyl-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone, or a pharmaceutically acceptable salt thereof.

18. A pharmaceutical composition for treating an inflammatory disease susceptable to treatment with an non-steroidal anti-inflammatory agent comprising:

a non-toxic therapeutically effective amount of a compound according to claim 1 and a pharmaceutically acceptable carrier.

19. A pharmaceutical composition for treating cyclooxygenase mediated diseases advantageously treated by an active agent that selectively inhibits COX-2 in preference to COX-1 comprising:

a non-toxic therapeutically effective amount of a compound according to claim **1** and a pharmaceutically acceptable carrier.

20. A pharmaceutical composition for treating an inflammatory disease susceptable to treatment with an non-steroidal a-ntiinflammatory agent comprising:

a non-toxic therapeutically effective amount of a compound according to claim **17** and a pharmaceutically acceptable carrier.

21. A pharmaceutical composition for treating cyclooxygenase mediated diseases advantageously treated by an active agent that selectively inhibits COX-2 in preferencc to COX-1 comprising:

a non-toxic therapeutically effective amount of a compound according to claim **17** and a pharmaceutically acceptable carrier.

22. A method of treating an inflammatory disease susceptable to treatment with an non-steroidal anti-inflammatory agent comprising:

administration to a patient in need of such treatment of a non-toxic therapeutically effective amount of a compound according to claim **1** and a pharmaceutically acceptable carder.

23. A method of treating cyclooxygenase mediated diseases advantageously treated by an active agent that selectively inhibits COX-2 in preference to COX-1 comprising:

administration to a patient in need of such treatment of a non-toxic therapeutically effective amount of a compound according to claim **1.**

24. A method of treating an inflammatory disease susceptable to treatment with an non-steroidal anti-inflammatory agent comprising:

administration to a patient in need of such treatment of a non-toxic therapeutically effective amount of a compound according to claim **17** and a pharmaceutically acceptable carrier.

25. A method of treating cyclooxygenase mediated diseases advantageously treated by an active agent that selectively inhibits COX-2 in preferencc to COX-1 comprising: administration to a patient in need of such treatment of a non-toxic therapeutically effective amount of a compound according to claim 17.

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